

REPLACEMENT SHEET

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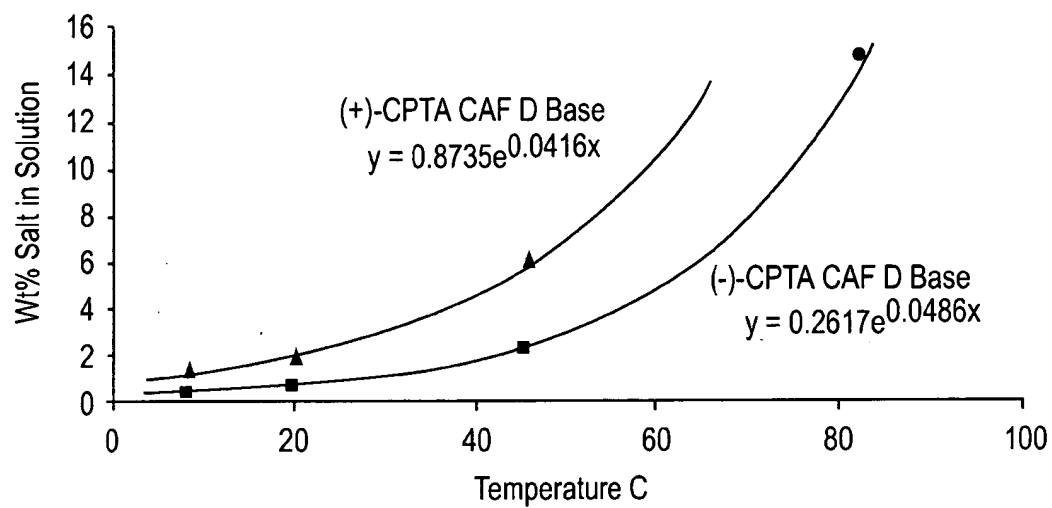


FIG. 1

REPLACEMENT SHEET

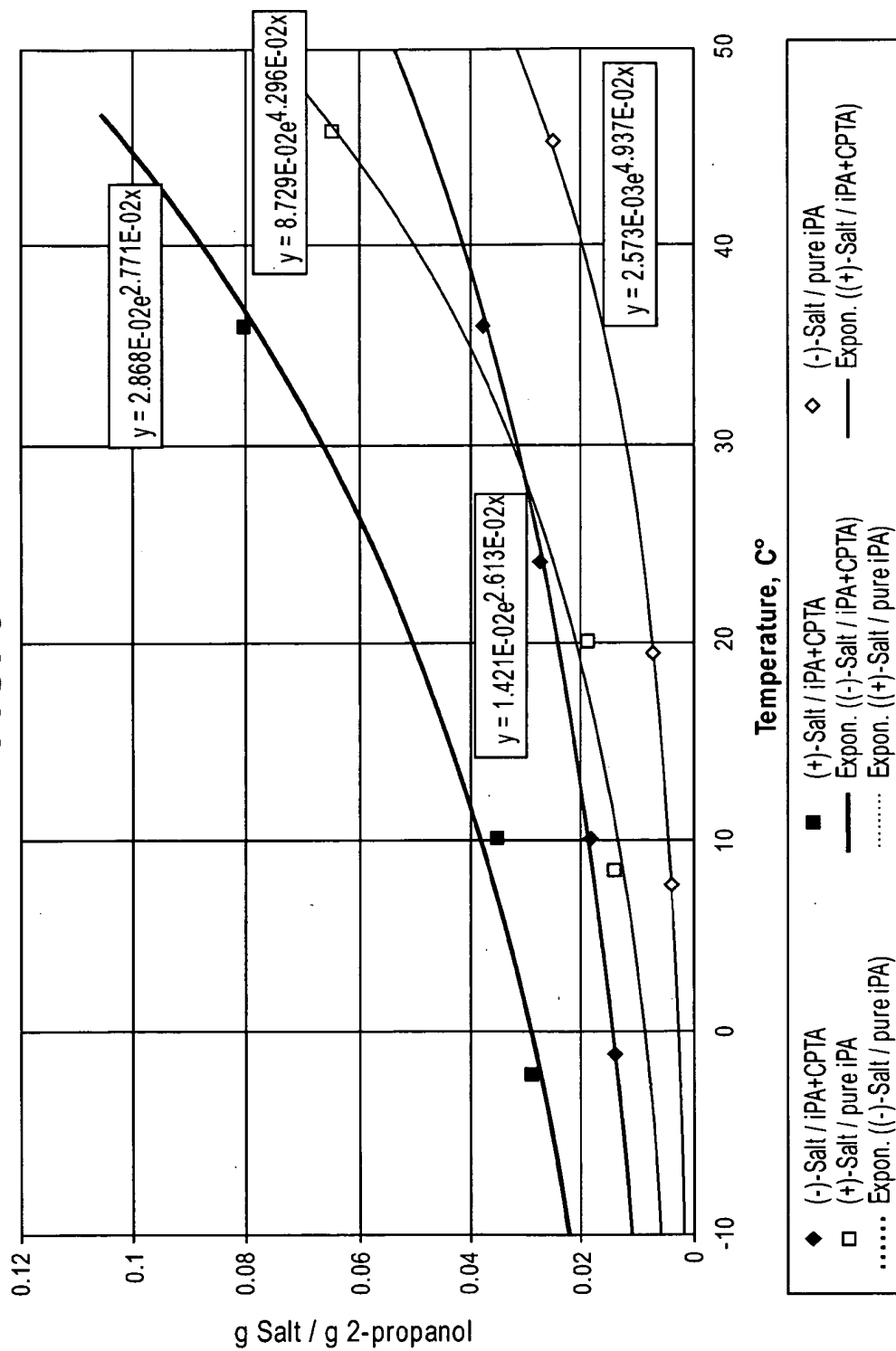
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| Exp. # | Charge | | Nucl'n Temp. | Isolation Temp & Hold Time | Product Isolation: Ratio of % (-)-CPTA | | Calculated % Yield of (-)-CPTA | Comments |
|--------|-----------------|-------------------------|--------------|----------------------------|---|------|--------------------------------|---|
| | g IPA/ gCPTA | mole base/ mole CPTA | | | Crystal | M.L. | | |
| 1 | 4.11 | 0.57 | 61° | 17° + 6hr | 79.9 | 27.0 | 69.5 | (+)-Salt nucleation at 22° |
| 2 | 4.11 | 0.55 | 59° | 22° + 8hr | 77.9 | 28.3 | 68.2 | (+)-Salt nucleation after 1 hr at 22° |
| 3 | 4.11 | 0.90 | 59° | 40° | 99.2 | 27.7 | 61.9 | initially added 0.15 eq. triethylamine |
| 4 | 5.50 | 0.75 | 61° | 22° + 10hr | 66.4 | 30.7 | 71.8 | (+)-Salt nucleation at 40° |
| | | | | to 28° | 68.2 | 28.8 | 73.4 | |
| | | | | to 35° | 71.4 | 29.1 | 70.6 | |
| | | | | to 43° | 77.0 | 29.9 | 65.7 | |
| | | | | to 51° | 95.0 | 30.3 | 57.9 | |
| | | | | to 55° | 99.4 | 33.0 | 50.9 | |
| 5 | 4.11 | 0.52 | 61° | 13° + 8hr | 99.7 | 20.9 | 73.6 | (+)-Salt nucleation 3 hr after sample |
| | | | | +30hr(13°) | 83.3 | 24.9 | 71.6 | |
| 6 | 3.14 | 0.52 | 59° | 1° | 98.7 | 23.5 | 69.6 | |
| | | | | +20hr(1°) | 98.2 | 19.4 | 76.3 | |
| | | | | to 17° + 9hr | 81.2 | 25.3 | 71.8 | |
| 7 | 5.50 | 0.90 | 64° | 3° + 1hr | 66.4 | 25.5 | 79.6 | initially added 0.04 eq. KOH |
| | | | | to 22° + 10hr | -56 | 25.5 | 90.0 | |
| 8 | 3.53 | 0.55 | 59° | 22° + 5hr | 78.6 | 26.0 | 71.7 | (+)-Salt nucleation at 30° |
| 9 | 3.93 | 0.45 | 59° | 22° + 4hr | 99.6 | 24.3 | 68.0 | |
| | | | | + 12hr (22°) | 99.5 | 22.9 | 70.4 | |
| | | 0.52 (added base) | | (22°) + 3hr | 89.4 | 24.6 | 70.1 | (+)-Salt nucleating, not at equilibrium |
| | | 0.49 (added CPTA) | | (22°) + 22hr | 84.3 | 25.9 | 69.6 | |
| 10 | 3.53 | 0.52 | 59° | 22° + 10hr | 73.9 | 25.5 | 74.8 | (+)-Salt nucleation at 25° |
| 11 | 3.93 | 0.45 | 54° | 22° + 14hr | 99.1 | 22.6 | 71.0 | |
| | | 0.48 (added base) | | 22° + 24hr | 89.2 | 24.7 | 70.0 | |
| 12 | 3.93 | 0.43 | 52° | 21° | 99.5 | 27.5 | 62.2 | |
| | | | | + 16hr(21°) | 99.4 | 23.9 | 68.7 | seeded with (+)-Salt after sample |
| | | | | +8hr(22°) | 99.3 | 23.7 | 69.1 | |
| | | 0.45 (added base) | | 22° + 14hr | 98.9 | 22.5 | 71.2 | seeded with (+)-Salt after sample |
| | | | | +6hr(22°) | 98.7 | 22.3 | 71.61 | |
| | | 0.47 (added base) | | 22° + 14hr | 96.8 | 21.9 | 72.6 | seeded with (+)-Salt after sample |
| | | | | + 23hr(22°) | 92.3 | 23.4 | 71.3 | |
| 13 | 3.14 | 0.38 | 59° | 17° + 8hr | 99.4 | 27.2 | 62.8 | |
| | | | | to -10° + 19hr | 99.8 | 24.3 | 67.9 | seeded with (+)-Salt after reaching 10° |

FIG. 2

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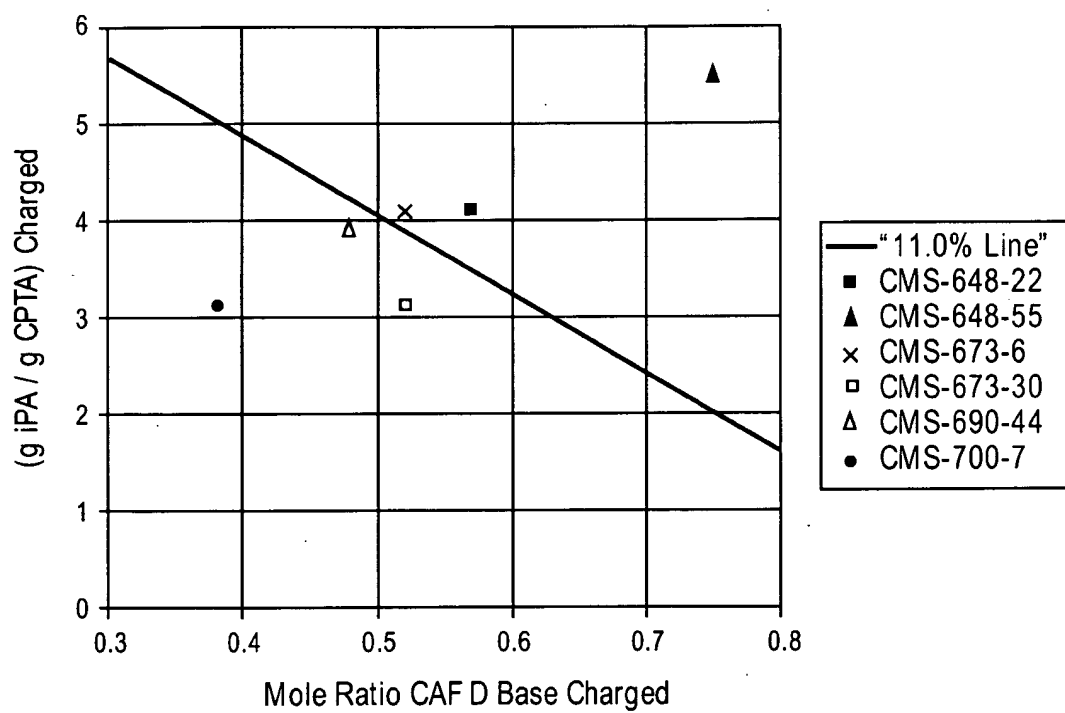
FIG. 3



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FIG. 4



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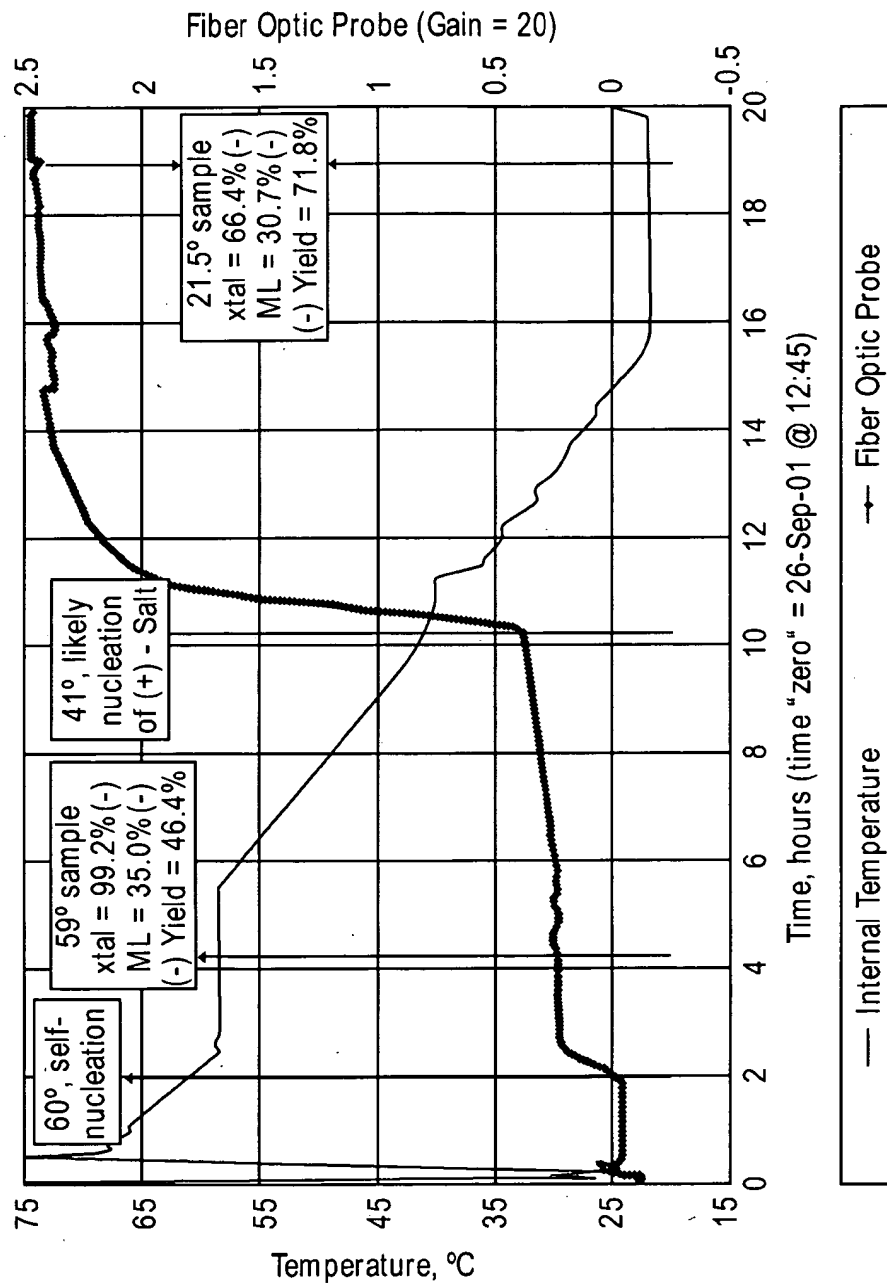


FIG. 5

REPLACEMENT SHEET

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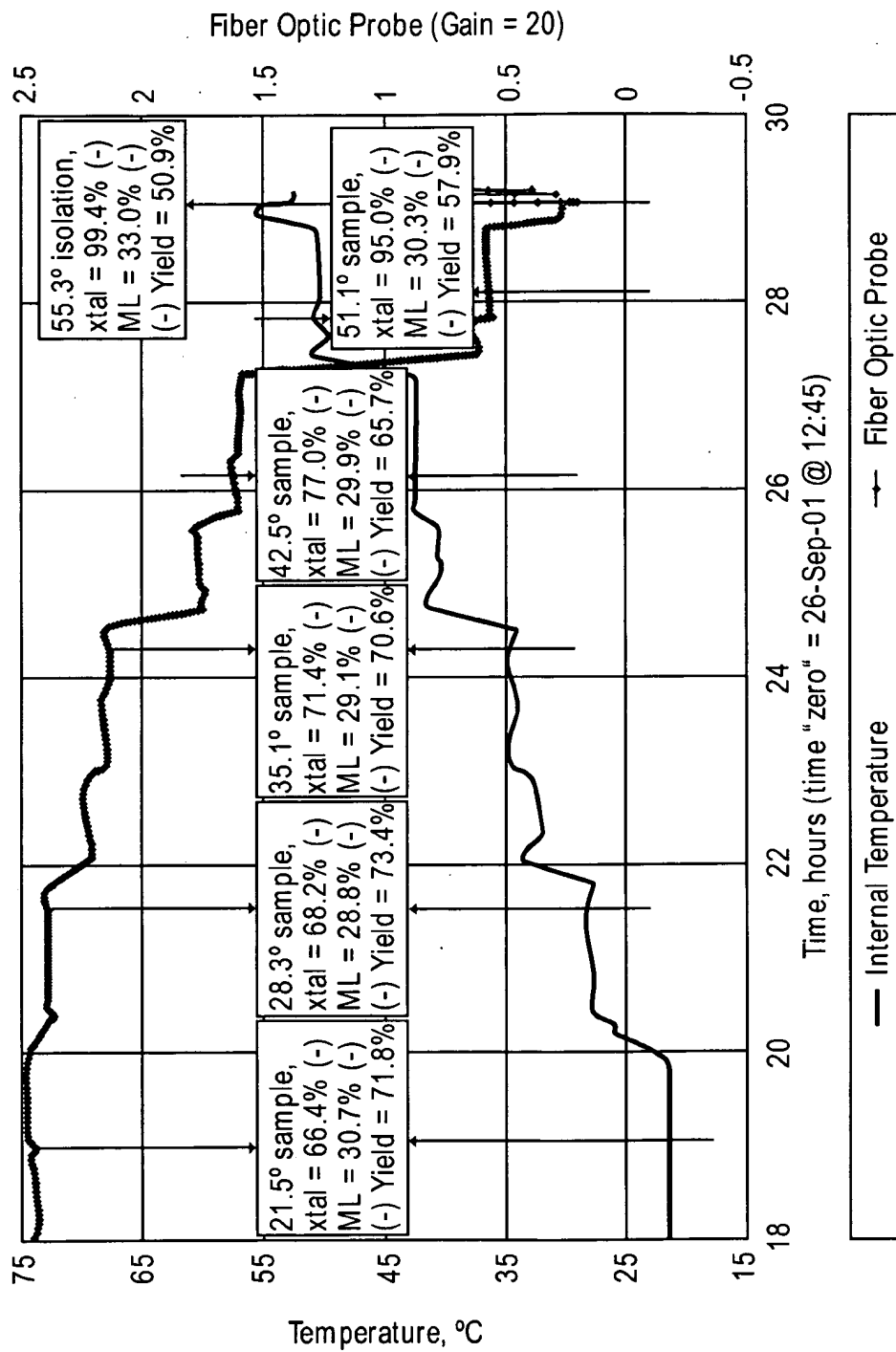


FIG. 5 (CONT.)

REPLACEMENT SHEET

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| Temperature | Measured Component | Experimental Result | Calculation By Model |
|-------------|-------------------------------------|---------------------|----------------------|
| 21.5 °C | Ratio % (-) - CPTA in crystal | 66.4% | 63.9% |
| | Ratio % (-) - CPTA in mother liquor | 30.7% | 28.5% |
| | % (-) - CPTA yield | 71.8% | 72.8% |
| | | | |
| 28.3 °C | Ratio % (-) - CPTA in crystal | 68.2% | 68.2% |
| | Ratio % (-) - CPTA in mother liquor | 28.8% | 28.7% |
| | % (-) - CPTA yield | 73.4% | 73.6% |
| | | | |
| 35.1 °C | Ratio % (-) - CPTA in crystal | 71.4% | 71.4% |
| | Ratio % (-) - CPTA in mother liquor | 29.1% | 28.9% |
| | % (-) - CPTA yield | 70.6% | 70.8% |
| | | | |
| 42.5 °C | Ratio % (-) - CPTA in crystal | 77.0% | 76.7% |
| | Ratio % (-) - CPTA in mother liquor | 29.9% | 29.1% |
| | % (-) - CPTA yield | 65.7% | 67.4% |
| | | | |
| 51.1 °C | Ratio % (-) - CPTA in crystal | 95.0% | 87.3% |
| | Ratio % (-) - CPTA in mother liquor | 30.3% | 29.2% |
| | % (-) - CPTA yield | 57.9% | 62.4% |
| | | | |
| 55.3 °C | Ratio % (-) - CPTA in crystal | 99.4% | 96.1% |
| | Ratio % (-) - CPTA in mother liquor | 33.0% | 29.3% |
| | % (-) - CPTA yield | 50.9% | 59.6% |
| | | | |

FIG. 6

REPLACEMENT SHEET

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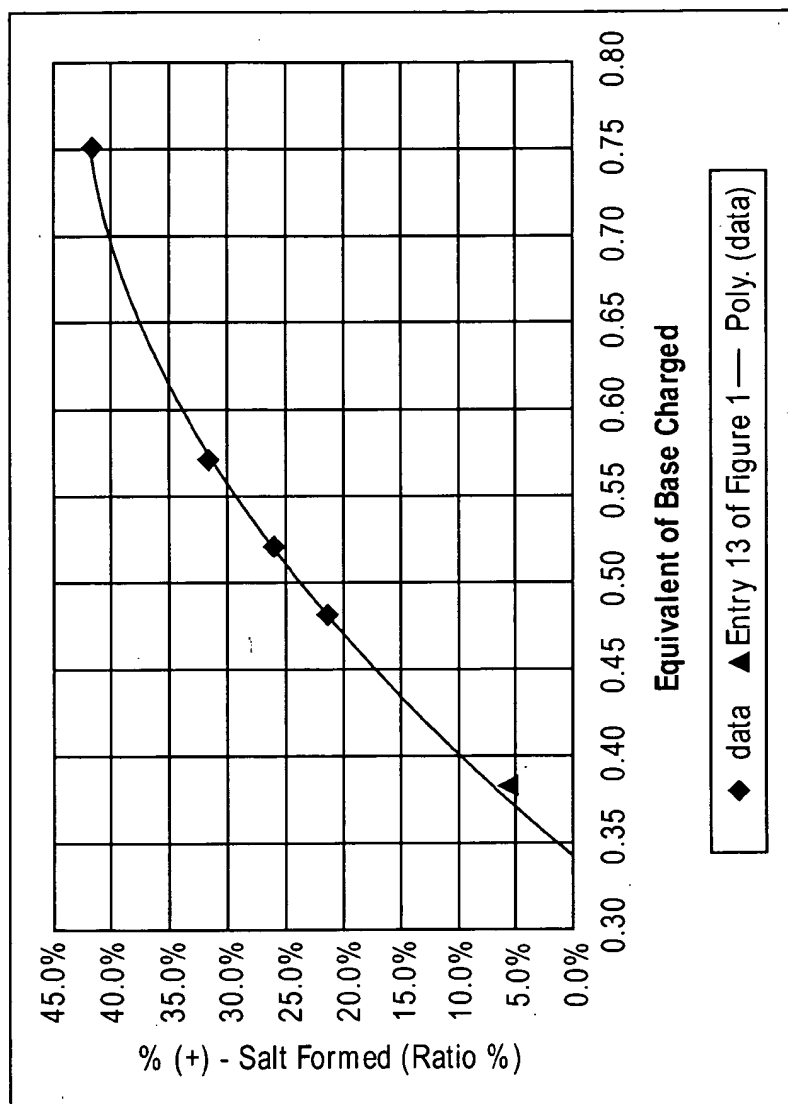


FIG. 7

REPLACEMENT SHEET

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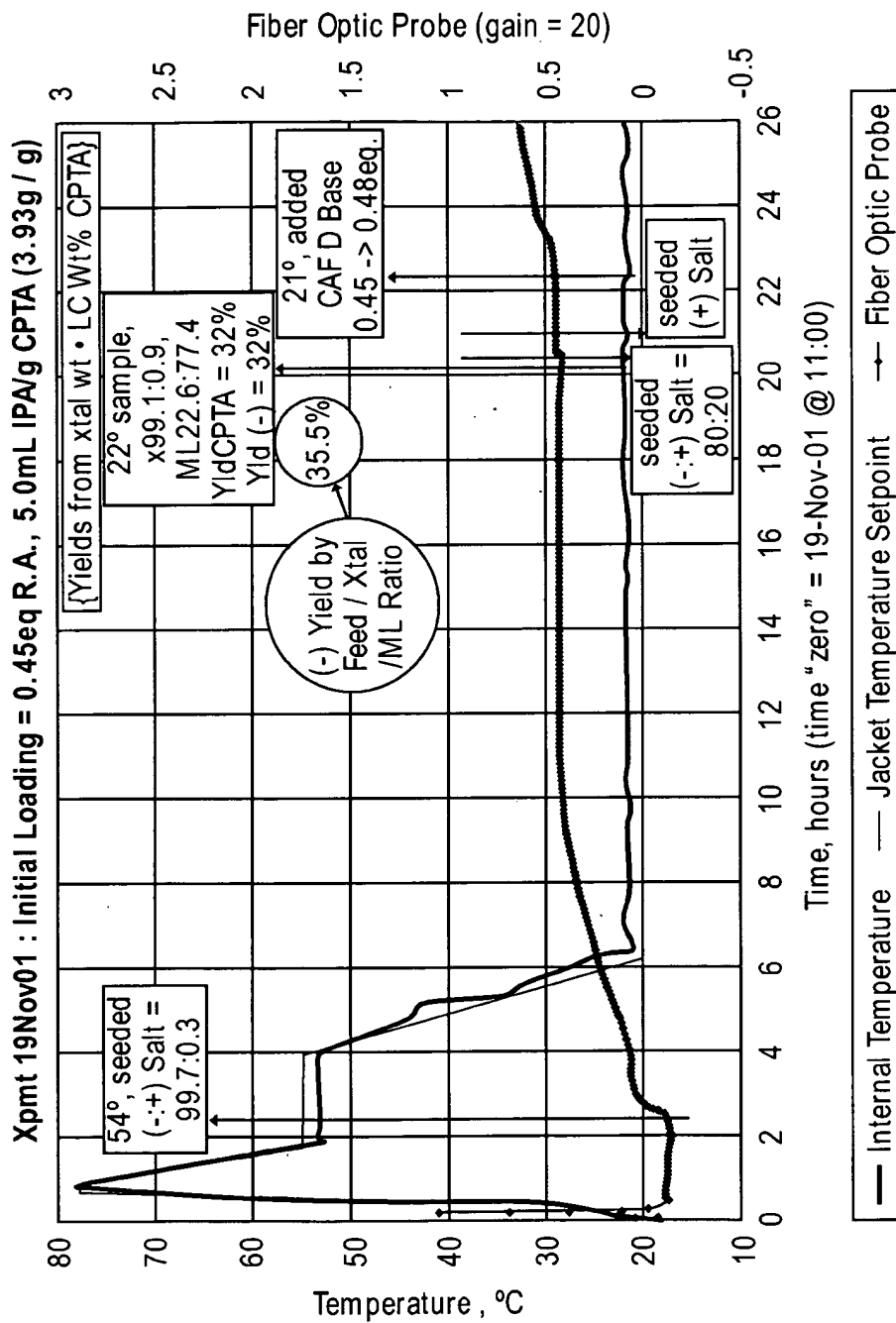


FIG. 8

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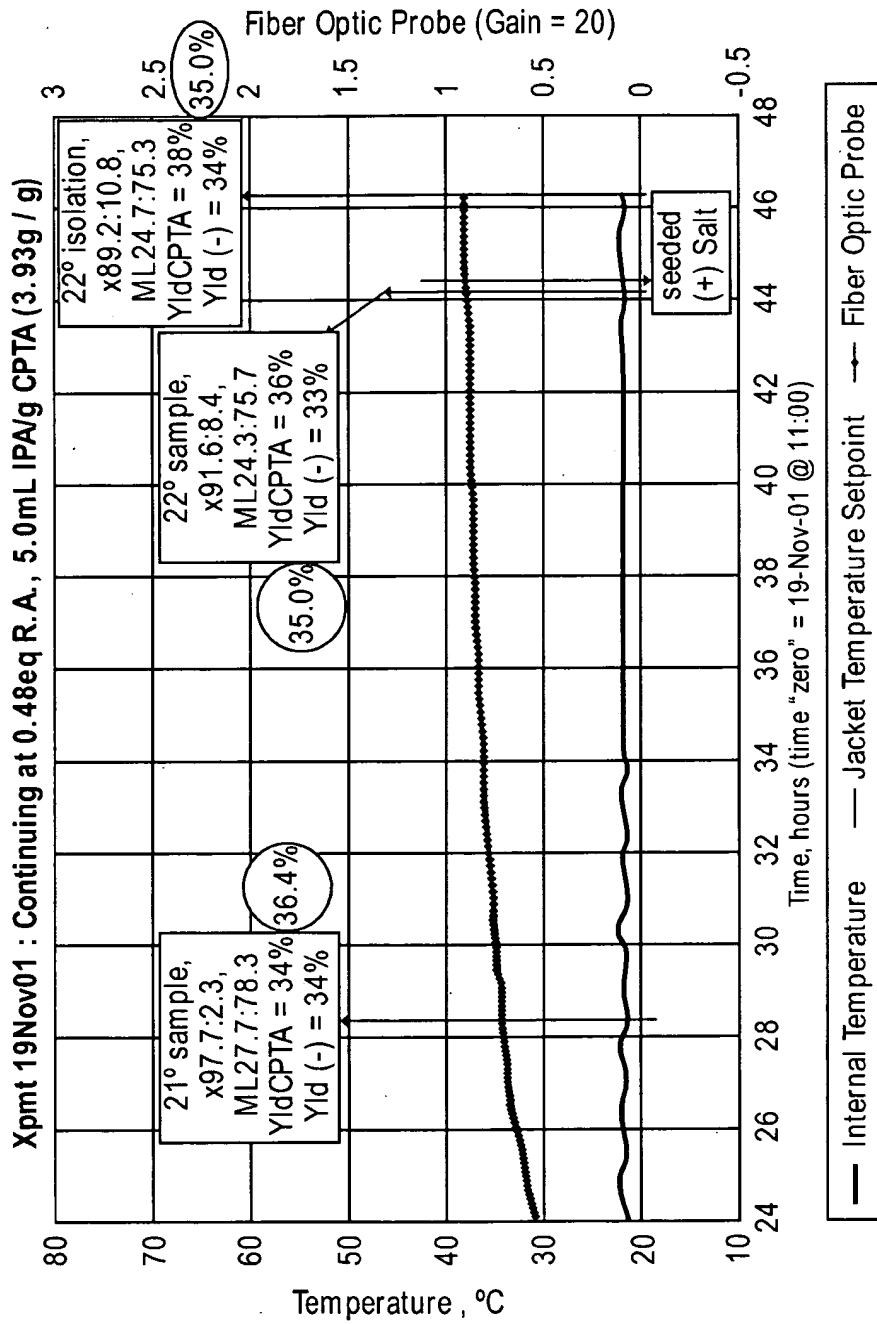


FIG. 8 (CONT.)

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| Component | Normalized Wt% (as CPTA) in Mother Liquor | |
|-----------|---|----------|
| | By Work-up | By Model |
| (-)-Salt | 28% | 20% |
| (+)-Salt | 41% | 44% |
| (-)-CPTA | 7% | 9% |
| (+)-CPTA | 24% | 27% |

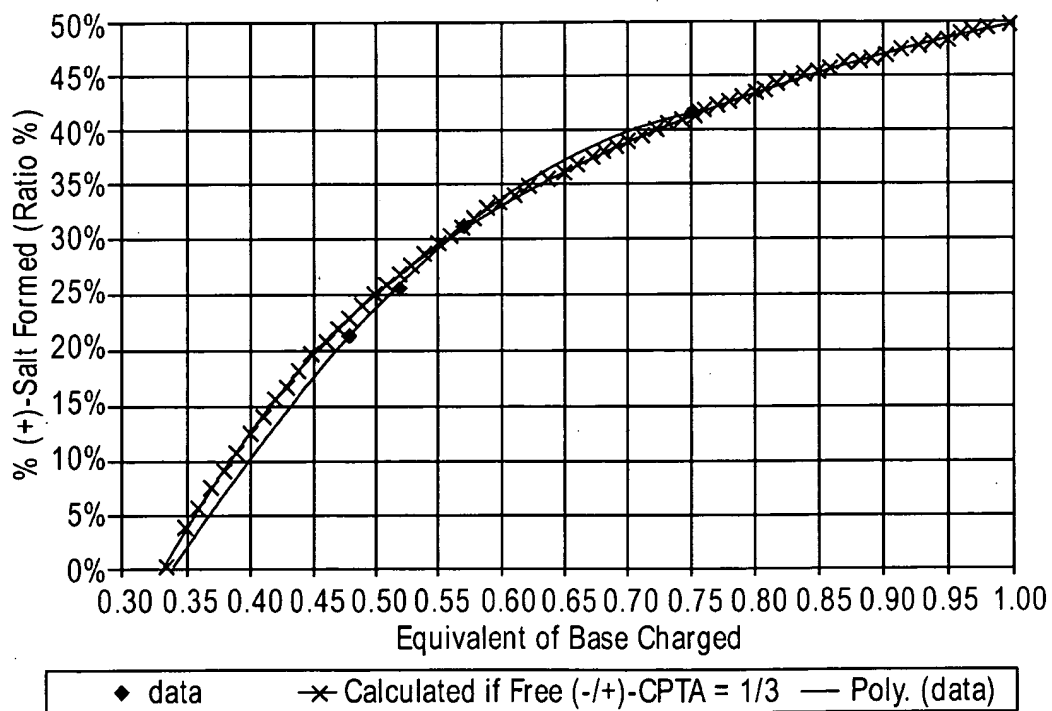


FIG. 9

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| (-)-CPTA • CAF D Base Salt m.p. 180.5 - 181.5 | | | | | | | | | | | | | |
|---|-------------|-------------------|-----------------|-----------------|---------------|----------------------|-----------------|---------------|-----------------|---------------|---------------------------|--------------------------|--------------------------|
| Solvent | Temp. °C | Calculated Values | | | | | | | | | | | |
| | | grams tare | grams w/soln | grams evap'd | grams soln | grams volat. solv | grams solids | grams CPTA | grams solute | Wt% solute | wt% solute in evapSolv | g solute/ g evap solv | g solute/ g evap solv |
| IPA w/CPTA | 36 | 17.2900 | 18.0100 | 17.3895 | 0.7200 | 0.6205 | 0.0935 | 0.0767 | 0.0228 | 3.17% | 3.55% | 0.036755 | |
| IPA w/CPTA | 24 | 16.7808 | 17.5728 | 16.8840 | 0.7920 | 0.6888 | 0.1032 | 0.0851 | 0.0181 | 2.28% | 2.56% | 0.026226 | |
| IPA w/CPTA | 10 | 17.2556 | 18.1769 | 17.3702 | 0.9213 | 0.8067 | 0.1146 | 0.0997 | 0.0149 | 1.62% | 1.81% | 0.01846 | |
| IPA w/CPTA | -1 | 17.1063 | 17.9898 | 17.2131 | 0.8835 | 0.7767 | 0.1068 | 0.0960 | 0.0108 | 1.22% | 1.37% | 0.013905 | |
| | | | | | | | | | | | | | |
| EtOH w/CPTA | 36 | 17.1900 | 17.9419 | 17.3577 | 0.7519 | 0.5842 | 0.1677 | 0.0912 | 0.0765 | 10.18% | 11.58% | 0.130959 | |
| EtOH w/CPTA | 24 | 17.2524 | 17.9330 | 17.3813 | 0.6806 | 0.5517 | 0.1289 | 0.0861 | 0.0428 | 6.29% | 7.20% | 0.077541 | |
| EtOH w/CPTA | 10 | 17.2977 | 18.1608 | 17.4587 | 0.8631 | 0.7021 | 0.1610 | 0.1096 | 0.0514 | 5.96% | 6.82% | 0.073212 | |
| EtOH w/CPTA | -1 | 17.1536 | 18.2098 | 17.3383 | 1.0562 | 0.8715 | 0.1847 | 0.1360 | 0.0487 | 4.61% | 5.29% | 0.066833 | |

| (+)-CPTA • CAF D Base Salt | | | | | | | | | | | | | |
|----------------------------|-------------|-------------------|-----------------|-----------------|---------------|------------------|-----------------|---------------|-----------------|---------------|---------------------------|--------------------------|--------------------------|
| Solvent | Temp. °C | Calculated Values | | | | | | | | | | | |
| | | grams tare | grams w/soln | grams evap'd | grams soln | grams solvent | grams solids | grams CPTA | grams solute | Wt% solute | wt% solute in evapSolv | g solute/ g evap solv | g solute/ g evap solv |
| IPA w/CPTA | -2 | 17.2325 | 17.8545 | 17.3147 | 0.6220 | 0.5398 | 0.0822 | 0.0667 | 0.0155 | 2.49% | 2.79% | 0.028679 | |
| IPA w/CPTA | 10 | 17.1810 | 17.7942 | 17.2649 | 0.6132 | 0.5293 | 0.0839 | 0.0654 | 0.0185 | 3.01% | 3.37% | 0.034911 | |
| IPA w/CPTA | 22 | 17.2838 | 18.0462 | 17.4053 | 0.7624 | 0.6409 | 0.1215 | 0.0792 | 0.0423 | 5.55% | 6.19% | 0.065977 | |
| IPA w/CPTA | 36 | 17.1474 | 17.8976 | 17.2742 | 0.7502 | 0.6234 | 0.1268 | 0.0771 | 0.0497 | 6.63% | 7.39% | 0.079801 | |
| | 10 | 17.2816 | 17.4692 | 17.3074 | 0.1876 | 0.1618 | 0.0258 | 0.0200 | 0.0058 | 3.09% | 3.46% | 0.035856 | |
| | | | | | | | | | | | | | |
| EtOH w/CPTA | -2 | 17.3289 | 18.5380 | 17.6105 | 1.2091 | 0.9275 | 0.2816 | 0.1448 | 0.1368 | 11.32% | 12.85% | 0.147512 | |
| EtOH w/CPTA | 10 | 17.2118 | 17.9940 | 17.4089 | 0.7822 | 0.5851 | 0.1971 | 0.0913 | 0.1058 | 13.52% | 15.31% | 0.180765 | |
| EtOH w/CPTA | 22 | 17.2095 | 18.0054 | 17.4362 | 0.7959 | 0.5692 | 0.2267 | 0.0889 | 0.1378 | 17.32% | 19.50% | 0.242178 | |
| EtOH w/CPTA | 36 | 17.2133 | 17.9657 | 17.4487 | 0.7524 | 0.5170 | 0.2354 | 0.0807 | 0.1547 | 20.56% | 23.03% | 0.299219 | |

FIG. 10A

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| Eq. Base | Predicted k | Regression k used | Regression % (+)-Salt | Free CPTA, Ratio % (+) |
|-------------|------------------|------------------------|--------------------------|---------------------------|
| 0.75 | <1 | 0.68 | 41.9 | 25.8 |
| | | | | |
| 0.57 | <1 | 0.85 | 31.4 | 25.3 |
| | | | | |
| 0.52 | <1 | 0.70 | 25.7 | 23.7 |
| 0.52 | >1 | 0.60 | 26.1 | 24.1 |
| | | | | |
| 0.48 | >1 | 0.50 | 21.5 | 23.7 |

Experimental Data for Figure 6

FIG. 10A (CONT.)

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[illegible]

FIG. 10B

REPLACEMENT SHEET

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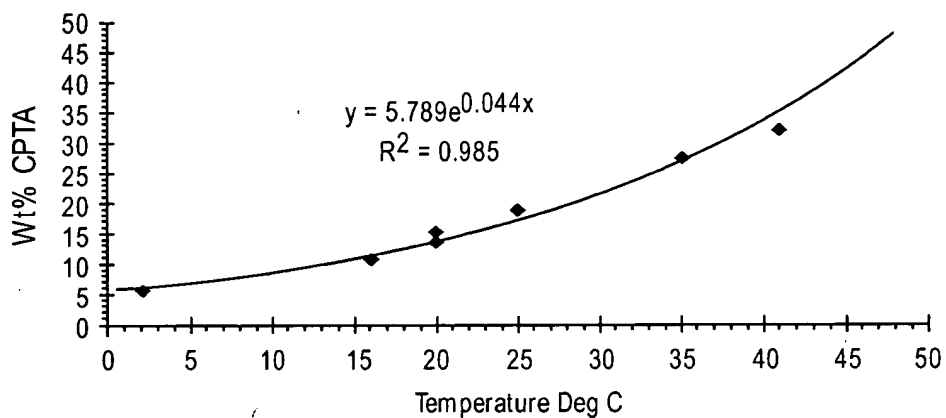


FIG. 11

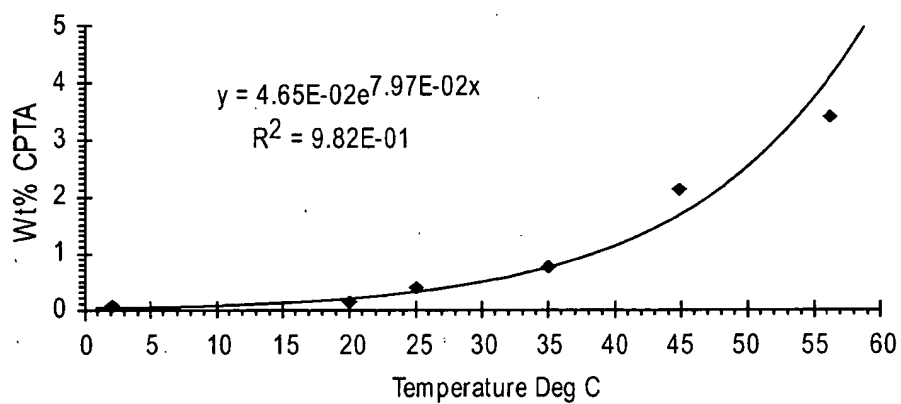


FIG. 12

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| Exp. # | MolRatio Base | g IPA/ g CPTA | Cool at °C/min | Final T °C | Solid % (-) | Solid % (+) | M.L. % (-) | M.L. % (+) | % Yield Calc | % Yield Overall | % Yield Actual |
|-------------------|------------------|------------------|-------------------|---------------|----------------|----------------|---------------|---------------|-----------------|--------------------|-------------------|
| 1 | 0.53 | 4.00 | 0.25 | 4 | 90.72 | 9.28 | 20.61 | 79.39 | 41.9 | | |
| Recrystallization | | 4.00 | 0.25-1.0 | 2 | 99.38 | 0.62 | 42.60 | 57.40 | 84.7 | 35.5 | 34.5 |
| 2 | 0.50 | 6.17 | 0.05 | -3 | 98.05 | 1.95 | 24.05 | 75.95 | 35.1 | 35.1 | 33.6 |
| 3 | 0.53 | 4.00 | 0.25 | 0 | 73.14 | 26.86 | 28.88 | 71.12 | 47.7 | | |
| Recrystallization | | 4.00 | 1.0 | 11 | 98.20 | 1.80 | 22.62 | 77.38 | 66.8 | 31.9 | 33.0 |
| 4 | 0.54 | 4.00 | 0.25 | -4 | 79.72 | 20.28 | 26.62 | 73.38 | 44.0 | | |
| Recrystallization | | 3.63 | 0.08 | 4 | 99.07 | 0.93 | 23.22 | 76.78 | 74.5 | 32.8 | 32.8 |
| 5 | 0.53 | 4.00 | 0.5 | -11 | 93.70 | 6.30 | 26.00 | 74.00 | 35.4 | | |
| Recrystallization | | 3.93 | 0.5 | -3 | 99.68 | 0.33 | 46.42 | 53.58 | 88.8 | 31.5 | 31.6 |
| 6 | 0.53 | 3.98 | 0.25 | -3 | 90.88 | 9.12 | 26.95 | 73.05 | 36.1 | | |
| Recrystallization | | 4.98 | 0.1 | 4 | 99.42 | 0.58 | 23.85 | 76.15 | 88.7 | 32.0 | 31.5 |
| 7 | 0.54 | 4.08 | 0.3 | -3 | 96.00 | 4.00 | nd | nd | - | | |
| Recrystallization | | 4.24 | 0.4 | 4 | 99.86 | 0.14 | 57.41 | 42.59 | 90.9 | - | 31.2 |
| 8 | 0.53 | 4.00 | 0.25 | -8 | 73.54 | 26.46 | 28.09 | 71.91 | 48.2 | | |
| Recrystallization | | 3.96 | 0.3 | 11 | 98.57 | 1.43 | 21.84 | 78.16 | 67.4 | 32.5 | 31.1 |
| 9 | 0.50 | 3.88 | 0.08 | -7 | 76.83 | 23.17 | 28.96 | 71.04 | 43.9 | | |
| Recrystallization | | 4.62 | 0.5 | 5 | 98.48 | 1.52 | 24.91 | 75.09 | 70.6 | 31.0 | 30.7 |
| 10 | 0.50 | 3.90 | 0.05 | 0 | 96.15 | 3.85 | 26.07 | 73.93 | 34.1 | | |
| Recrystallization | | 4.80 | 0.3 | 3 | 99.86 | 0.14 | 70.32 | 29.68 | 87.4 | 29.9 | 30.6 |
| 11 | 0.55 | 6.16 | 0.2 | 5 | 73.92 | 26.08 | nd | nd | - | | |
| Recrystallization | | 4.38 | 0.08 | 12 | 99.31 | 0.69 | 41.08 | 58.92 | 56.4 | - | 29.1 |
| 12 | 0.56 | 4.99 | 0.1 | 2 | 78.92 | 21.08 | 28.04 | 71.96 | 43.2 | | |
| Recrystallization | | 5.00 | 0.25 | 4 | 84.47 | 15.53 | 29.29 | 70.71 | 89.9 | (38.8) | (38.3) |
| Recrystallization | | 5.00 | 0.25 | 12 | 99.44 | 0.56 | 30.30 | 69.70 | 78.4 | 30.4 | 28.2 |

nd - Not Determined

FIG. 13

| Exp. # (Fig. 1) | Initial T °C | Rate °C/min | Final T °C | Hrs at < 10 °C | Holding Period Profile | Solid | | M.L. | | % Yield (-)-CPTA |
|--------------------|-----------------|----------------|---------------|-------------------|-------------------------------------|-------|-------|-------|-------|---------------------|
| | | | | | | % (-) | % (+) | % (-) | % (+) | |
| 1 | 60 | 0.25 | 4 | 14 | 13h at 4C | 90.72 | 9.28 | 20.61 | 79.39 | 38.0 |
| 8 | 60 | 0.25 | -5 | 20 | 11h to 10C, 3h to -8C, 5h at -8C | 73.54 | 26.46 | 28.09 | 71.91 | 35.5 |
| 4 | 55 | 0.25 | -4 | 3 | 1h at -4C | 79.72 | 20.28 | 26.62 | 73.38 | 35.1 |
| 3 | 60 | 0.25 | -2 | 16 | 11h to 10C, 1h to -2C, 4h at -2C | 73.14 | 26.86 | 28.88 | 71.12 | 34.9 |
| 2 | 55 | 0.05 | -3 | 5 | 1h at -3C | 98.05 | 1.95 | 24.05 | 75.95 | 34.4 |
| 12 | 55 | 0.10 | 1 | 13 | 9h to 10C, 1h to 1C, 4h at 1C | 78.92 | 21.08 | 28.04 | 71.97 | 34.1 |
| 9 | 65 | 0.075 | 0 | 8 | 3h at 0C, 1h to -7C, 2h at -7C | 76.83 | 23.17 | 28.96 | 71.04 | 33.8 |
| 5 | 60 | 0.5 | -11 | 2.5 | 1.5h at -11C | 93.70 | 6.30 | 26.00 | 74.00 | 33.2 |
| 10 | 55 | 0.05 | 0 | 4 | 1h at 0C | 96.15 | 3.85 | 26.07 | 73.93 | 32.8 |
| 5 | 55 | 0.25 | -3 | 2 | 1h at -3C | 90.88 | 9.12 | 26.95 | 73.05 | 32.8 |

FIG. 14

| | %ee | | HPLC Area% Crude | | HPLC Area% Isolated | | Yield | mol % in ML | |
|-------------|------|----------------|------------------|------------|---------------------|------------|-------|-------------|------------|
| | CPTA | (-)-halofenate | CPTA | Halofenate | CPTA | Halofenate | | CPTA | Halofenate |
| 1 | 97.1 | 99.9 | 6.1 | 85.2 | 0.72 | 98.93 | 55% | 5.8% | 38% |
| 2 | 99.3 | >99.8 | 5.5 | 89.6 | 0.60 | 99.40 | 52% | 5.9% | 41% |
| Second Crop | 99.6 | | 6.1 | 45.0 | 3.89 | 89.93 | 21% | 4.3% | 13% |
| 3 | 99.2 | 99.7 | 7.1 | 85.3 | 0.40 | 99.29 | 55% | 7.5% | 34% |
| 4 | 98.6 | 99.8 | 3.9 | 91.8 | 0.10 | 99.90 | 47% | 3.1% | 40% |
| Second Crop | 98.8 | | 6.1 | 82.5 | 3.22 | 89.65 | 33% | nd | nd |
| 5 | 99.7 | 99.7 | 8.0 | 83.2 | 0.64 | 99.18 | 59% | nd | nd |

nd - Not Determined

FIG. 15

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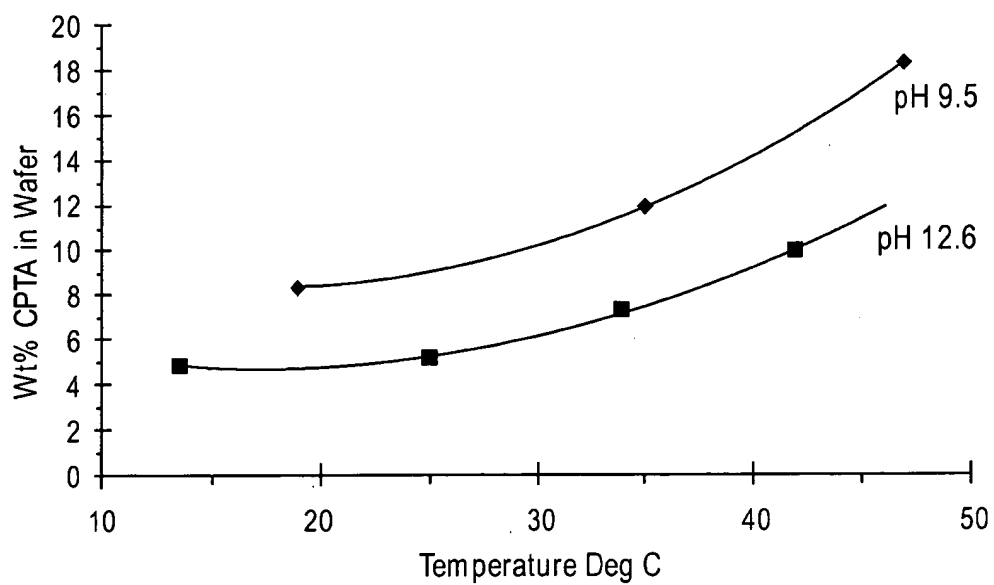


FIG. 16

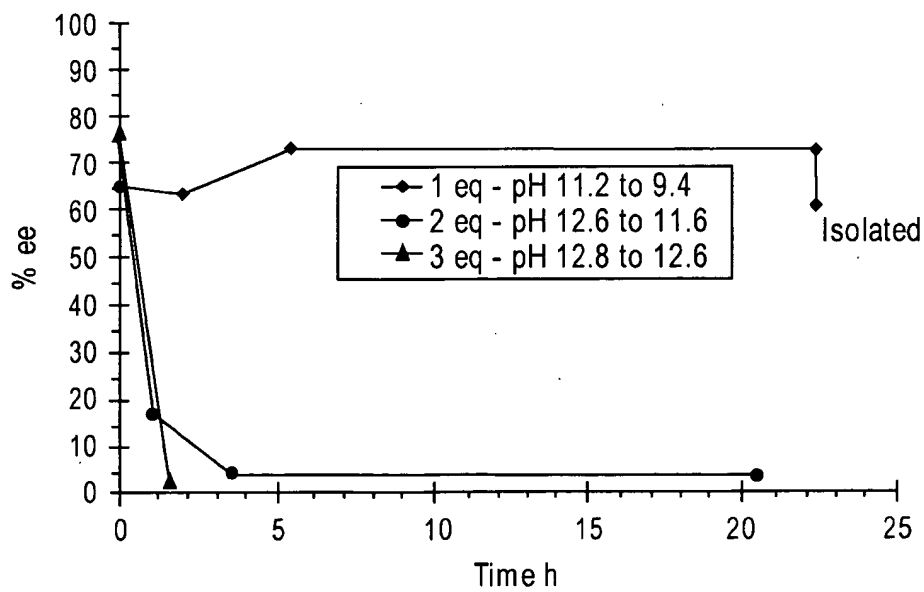


FIG. 17

REPLACEMENT SHEET

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| Recovered From: | Wt% Aqueous Soln | pH | mp °C | Recovery | (+)/(-) Ratio |
|---------------------|-------------------------|------|-------------|----------|---------------|
| Diastereomeric Salt | 20.4 | 12.4 | 157.2-158.0 | 97% | 0.1/99.9 |
| " | 20.1 | 12.1 | 160.4-161.0 | 98% | |
| " | 19.6 | nd | 164.0-164.6 | 92% | |
| " | 11.9 | 13.2 | 161.8-162.6 | 94% | |
| " | 4.1 | 12 | 164.0-164.6 | 88% | 0.1/99.9 |
| Resolution ML | 13.9 | 13 | 159.2-159.6 | 62% | |
| " | 11.0 | 12.3 | 162.4-163.0 | 87% | |
| Combined ML & Salt | 19.9 | 13 | 162.6-163.4 | 85% | |
| | TCI Americas Lot# FHG01 | | 165.6-166.4 | | 0.1/99.9 |

FIG. 18

| Solvent | Temp °C | Sample weight g | Sample Volume mL | Wt% CPTA in Solution |
|--------------------|---------|-----------------|------------------|----------------------|
| 1,2-Dichloroethane | 41 | 0.1558 | 25.00 | 32.3 |
| | 35 | 0.1360 | 25.00 | 27.6 |
| | 25 | 0.1455 | 10.00 | 18.8 |
| | 20 | 0.0489 | 25.00 | 15.3 |
| | 20 | 0.0505 | 10.00 | 14.0 |
| | 16 | 0.3230 | 25.00 | 11.0 |
| | 2.1 | 0.1300 | 10.00 | 6.05 |
| Heptane | 56 | 0.4641 | 25.00 | 3.39 |
| | 45 | 0.3331 | 25.00 | 2.11 |
| | 35 | 0.3823 | 25.00 | 0.767 |
| | 25 | 0.6750 | 25.00 | 0.413 |
| | 20 | 0.1994 | 10.00 | 0.17 |
| | 2.1 | 0.6038 | 25.00 | 0.057 |

FIG. 19

| pH | Temp °C | Sample weight g | Sample Volume mL | Wt% CPTA in Solution |
|------|---------|-----------------|------------------|----------------------|
| 9.4 | 35 | 0.3036 | 25.00 | 11.86 |
| 9.7 | 47 | 0.1111 | 25.00 | 18.28 |
| 9.5 | 19 | 0.2290 | 25.00 | 8.33 |
| 12.7 | 13.5 | 0.2012 | 25.00 | 4.89 |
| 12.6 | 25 | 0.3538 | 25.00 | 5.18 |
| 12.5 | 34 | 0.2320 | 25.00 | 7.30 |
| 12.5 | 42 | 0.3055 | 25.00 | 9.91 |

FIG. 20

| (+) - Halofenate | Wt Loaded g | | Reflux Time | pH | HPLC Area% (+) / (-) | % CPTA | |
|------------------|-------------|------|-------------|-----------|-------------------------|--------|----------|
| | 50% NaOH | | | | | Assay | Isolated |
| 8.65 | 1.67 (1 eq) | 0 h | 11.2 | 71.9/15.1 | | | |
| | | 2 | | 78.3/17.2 | | | |
| | | 5.5 | | 80.6/12.4 | | | |
| | | 22.5 | 9.4 | 84.1/13.4 | | | |
| | | Oil | | 80.3/19.6 | 92% | 81% | |
| 6.94 | 2.68 (2 eq) | 0 | 12.6 | 83.4/11.3 | | | |
| | | 1 | | 56.8/40.4 | | | |
| | | 3.5 | | 49.0/45.0 | | | |
| | | 20.5 | 11.6 | 47.5/45.0 | | | |
| | | Oil | | 48.7/51.0 | 103% | 94% | |
| 7.28 | 4.21 (3 eq) | 0 | 12.8 | 80.4/10.5 | | | |
| | | 1.5 | 12.6 | 49.6/47.0 | | | |
| | | Oil | | 47.3/52.5 | 102% | 88% | |

FIG. 21